Supporting Online Material

MATERIALS AND METHODS

Expression constructs, mutagenesis and cell lines

The pcDNA3-Flag (-HA and-Myc) API2-MALT1 constructs were described previously (1, 2). For the API2-MALT1 fusion present in these constructs, the breakpoint for API2 corresponds to nucleotide 1323 of the cDNA sequence (AA residue 441), whereas the breakpoint for MALT1 corresponds to nucleotide 649 of the cDNA sequence (AA residue 217). These specific breakpoints represent the majority of clinically observed API2-MALT1 fusions (3). The resulting fusion protein contains three API2 BIR domains, one MALT1 Ig-like domain and the MALT1 "caspase-like" domain. The expression plasmids pcDNA3-Flag-API2(1-441), pcDNA3-Flag-MALT1(324-813), pcDNA3-Flag-E46A/R48A-API2-MALT1, pcDNA3-Flag-(D1-49)API2-MALT1, pcDNA3-Flag-(D1-98)API2-MALT1, pcDNA3-Flag-(D1-166)API2-MALT1, pcDNA3-HA-MALT1, pcDNA3-Myc-Bcl10, pcDNA3-Flag-API2-MALT1(1-762) and pcDNA3-Flag-API2-MALT1(1-700) were constructed as described previously (1, 2, 4). pcDNA-Flag-p100 and pcDNA3-HA/Flag-NIK were provided by Dr. Gabriel Nunez. Point mutants of API2-MALT1 (C678A) and NIK (KK429/430AA, R325A, R366A, and R368A) were prepared using the QuickChange XL Site-Directed Mutagenesis Kit (Stratagene, Cedar Creek, TX, USA). Expression constructs encoding NIK fragments (AAs 624-947, 1-325, and 326-947) were generated by polymerase chain reaction and then subcloned into the XbaI and ApaI sites of the corresponding pcDNA3 vector (Invitrogen, Carlsbad, CA, USA). NIK(624-947) is a dominant negative mutant that retains IKKa binding but lacks the kinase domain, and NIK KK429/430AA is a kinase-dead NIK dominant negative mutant. All DNA sequences were verified using an ABI Model 3730 automated sequencer.

HEK293T cells were obtained from American Type Culture Collection (ATCC, Manassas, VA, USA). The SSK41 lymphoma cell line with stable expression of A7M3, an API2-MALT1 fusion which contains three API2 BIR domains, two MALT1 Ig-like domains and the MALT1 "caspase-like" domain, has been previously described (5). BJAB B-cells that express API2-MALT1 or MALT1 from a tetracycline inducible promotor were generated as follows: First, a BJAB clone stably transfected with pTet-On (Clontech, Mountain View, CA, USA) was obtained from Dr. Rolf Renne (6). Next, these cells were transfected with pTRE2puro-Flag-API2-MALT1 or pTRE2puro-Flag-MALT1, and clones were selected for puromycin resistance and then screened for doxycyline-inducible expression of Flag-API2-MALT1 or Flag-MALT1 by Western blot.

Cell Culture, Transfection, and RNA interference

HEK293T cells were maintained in DMEM supplemented with 10% fetal bovine serum (FBS) according to standard procedures. A total of 5 X 10⁵ or 1 X 10⁶ HEK293T cells were transfected with indicated plasmids using either a calcium phosphate method or Lipofectamine 2000 (Invitrogen). BJAB cells were maintained at a concentration of 0.2 to 0.8 million cells/ml in RPMI 1640 with 10% FBS. Treatment with 1 μg/mL of doxycycline (Sigma-Aldrich, St. Louis, MO, USA) was used to induce expression of API2-MALT1 or MALT1. For analysis of the effect of B-cell receptor stimulation in BJAB cells, all cells were first stimulated with 1 μg/ml doxycycline for 24 hr, and then treated with or without 10 μg/ml Goat anti-human IgM as indicated for 5 hr. All cells were cultured in the presence of 25 μM MG132 for 5 hr prior to

harvest. SSK41 cells (7, 8) with stable expression of A7M3 were maintained in DMEM-F12 with 10% FBS plus 1 μ g/mL puromycin and 1.5 mg/mL G418 as described (5).

API2-MALT1-expressing SSK41 and BJAB B-cells were electroporated with control, human NIK-specific, IKKα-specific or IKKβ-specific siRNAs (ON-TARGET plus SMART pools, L-003580-00, L-003473-00, and L-003503-00, respectively, Dharmacon, Lafayette, CO) using Amaxa Cell Line Nucleofactor Kit T (Lonza Cologne AG, Germany) and program G16. Cells were allowed to recover for 48 hrs prior to further analysis. In order to generate clones with stable knock-down of NIK, API2-MALT1-expressing SSK41 B-cells were infected with control or NIK shRNA lentiviral particles (Santa Cruz Biotechnology, Santa Cruz, CA, sc-3606065 or sc-108080) at an MOI of 1 on two consecutive days. Infected cells were selected by limiting dilution in 96-well plates, and resultant clones were screened by western blot and/or RT-PCR to assess NIK knock-down.

Immunoprecipitation, nuclear fractionation, and Western blot analysis

Cells were harvested 24-48 hrs after transfection and lysed with RIPA buffer (Sigma-Aldrich) containing complete protease inhibitor (Roche Diagnostics, Mannheim, Germany). Immunoprecipitations were carried out using anti-FLAG antibody M2-Agarose (Sigma-Aldrich, #A2220) or anti-HA (Roche Laboratories, Basel, Switzerland, #11 583 816 001). immunoprecipitated products were resolved by SDS-PAGE and detected by Western blotting using ECL Western Blotting Substrate (Thermo Scientific, Rockford, IL, USA, #32106) or Lumagen TMA-6 (GE Healthcare UK Ltd., Buckinghamshire, England) according to the manufacturer's instructions. Cytoplasmic and nuclear extracts were prepared using the NE-PER Nuclear and Cytoplasmic Extraction Reagents according to the manufacturer's recommendations (Thermo Scientific, Rockford, IL, USA). Purity of the nuclear extracts was confirmed by Western blot for HDAC1. The following antibodies were used for Western Blot: anti-Flag M2peroxidase conjugate (Sigma-Aldrich, #A-8592), anti-Myc-HRP (Santa Cruz Biotechnology Inc., sc-40), anti-HA-HRP (Roche Laboratories, #11 667 475 5433), anti-HA (Roche Laboratories, #11 583 816 001), anti-p100/p52 (Cell Signaling Technology, Inc., Danvers, MA, USA, #4882), anti-RelB (Cell Signaling #4922), anti-NIK (Cell Signaling #4994, Santa Cruz Biotechnology #N-19, Santa Cruz Biotechnology #C-20), anti-MALT1 (9) or (Santa Cruz Biotechnology, H-300), anti-Bcl10 (Santa Cruz Biotechnology, sc-5611), anti-A20 (59A426, eBioscience, San Diego, CA, USA), anti-TRAF3 (Santa Cruz Biotechnology, sc-949), anti-IKKα (Santa Cruz Biotechnology, sc-949), anti-IKKβ (Santa Cruz Biotechnology, sc-7329-R), anti-Pim-2 (Santa Cruz Biotechnology, sc-13514), anti-phospho Serine 112-BAD (Cell Signaling # 9291), anti-BAFF (Abcam, Cambridge, MA, ab65360), anti-GAPDH (Santa Cruz Biotechnology, 6C5), anti-HDAC1 monoclonal antibody (Santa Cruz Biotechnology Inc.), goat-anti-rabbit-HRP (Jackson Laboratories, West Grove, PA, USA, #111-035-046), goat-anti-mouse-HRP (Jackson Laboratories, # 115-035-071).

MALT1 protease assay

As a source of recombinant MALT1 protein, HKB11 cells (Bayer Corporation, ATCC Number CRL-12568) were generated with stable expression of MALT1 fused to an N-terminal combined StrepII-Flag tag (IBA BioTagnology, Gottingen, Germany). Cells were grown in suspension in 293 serum free medium (Invitrogen NV, Merelbeke, Belgium). The StrepII-tagged MALT1 fusion protein was purified on Strep-Tactin columns according to the manufacturer's recommendations using the One-STrEP-tag purification kit (IBA BioTagnology). The MALT1

protease assay was performed in 25 μ l buffer (pH 6.8) consisting of 50 mM MES, 150 mM NaCl, 10% (w/v) sucrose, 0.1% (w/v) CHAPS, 10 mM dithiothreitol and 1 M (NH₄)₃citrate, supplemented with 100 μ M fluorogenic substrate (Ac-LSSR-AMC, Anaspec, Fremont, CA) and purified StrepII-tagged MALT1 fusion protein, with or without 100 μ M Ac-LSSR-CHO inhibitor. Time-dependent release of free amido-4-methylcoumarin (AMC) was measured on a FLUOstar Galaxy reader (BMG Labtechnologies GmbH, Offenburg, Germany), and activity was expressed as the increase of relative light units per minute per well.

NIK in vitro cleavage assay

A vector enabling expression of biotinylated NIK (pcD-NIK-V5-bioC) was constructed by introducing oligonucleotides encoding the biotinylation (bio) sequence (GLNDIFEAQKIEWHE) as described (10) downstream of a C-terminal V5 epitope in the plasmid pcDNA3.1. The bioimmunoprecipitation method was performed as described (5) using paramagnetic streptavidin beads (Dynabeads M-280, Invitrogen). In vitro cleavage assays were performed in 50 μ l kosmotropic salt buffer [50 mM MES (pH 6.8), 150 mM NaCl, 10% (w/v) sucrose, 0.1% (w/v) CHAPS, 10 mM dithiothreitol and 1 M (NH₄)₃citrate] in order to stabilize intermolecular interactions. Reactions were supplemented with streptavidin beads containing NIK-V5-bioC, StrepII/Flag-tagged MALT1, with or without 100 μ M Ac-LSSR-CHO inhibitor. After incubation at 37°C for 6 hrs with constant rotation, an aliquot of the reaction mixture was used for Western blotting with a Flag antibody to verify equal StrepII/Flag-MALT1 concentrations. The streptavidin beads were collected, washed with 1X PBS and boiled for 10 min in 1X SDS gel loading buffer (with a final concentration of 4% SDS and 300 mM β-mercaptoethanol) and western blotting was performed with the V5 antibody (sc-58052).

Dexamethasone-induced apoptosis assay

Dexamethasone was serially diluted in complete RPMI growth medium at the indicated concentrations in white Cliniplates (Labsource, Willowbrook, IL). The SSK41 B cells were plated at 40,000 cells per well. After 48 hrs, cell viability was assessed using the Cell Titer-Glo Luminescent Cell Viability Assay (Promega, Madison, WI) according to the manufacturer's recommendations. Values are calculated as a percentage of control cells receiving no treatment. P values were derived using a two-tailed T test.

B-cell adhesion assay

Adhesion assays were performed as described (11, 12). Briefly, BJAB B-cells with stable, doxycyline-inducible expression of Flag-API2-MALT1, or empty vector control BJAB cells were electroporated with control or NIK siRNA, followed by doxycycline treatment. 5X10⁵ cells were applied to 12 well plates (Becton-Dickinson) coated with BSA or VCAM-1, and then allowed to adhere for 30 min at 37°C. Plates were prepared by incubating for one hour at 37°C with 3 µg/ml VCAM-1 (R & D systems). Nonadherent cells were removed by washing with PBS. Three representative fields were then counted under 20X magnification. Adhesion was calculated as a % of input samples counted before washing. Each condition was performed in triplicate wells.

Quantitative RT-PCR Gene Expression Analyses

Control and API2-MALT1-expressing SSK41 cells were harvested and total RNA was then prepared using the RNAeasy Mini Kit (Qiagen). Equivalent amounts of RNA (500-1000 ng)

were used for cDNA synthesis with the Superscript First-Strand Synthesis System (Invitrogen) using oligo dT primers. Quantitative PCR was performed using TaqMan gene expression primers (Applied Biosystems) specific for human CXCR4, Pim-2, BAFF and integrin αL on an Applied Biosystems 7900HT apparatus supplied by the University of Michigan Microarray Core Facility. Cycle Thresholds were determined and normalized with those for reactions performed with GAPDH specific TaqMan primers. For each gene, relative expression was determined, setting a value of 1.0 for expression in control SSK41 cells. P values were derived using a two tailed T test.

Analysis of primary MALT lymphoma specimens

Cases of MALT lymphoma with known chromosomal translocation status were investigated by Western blot with anti-NIK, anti-p100/p52, and anti-C-terminal MALT1 antibody. The p52/p100 ratio was quantified by standard densitometric analysis. The use of archival human tissues for research was approved by the local research ethics committees of the authors' institutions.

Gene expression microarray analysis of two completely separate collections of MALT lymphoma tumor specimens was performed in order to determine if noncanonical NF-κB target genes are upregulated in tumors expressing API2-MALT1. Collection #1 included nine t(11;18)positive (8 from the stomach and 1 from lung) and eight t(11;18)-negative MALT lymphomas (all from the stomach). A description of these patient materials and the methodology for gene expression microarray analysis with Affymetrix GeneChip HG-U133A was detailed in a previous study (13) (GEO; http://www.ncbi.nlm.nih.gov/geo/, GSE16024). Standard normalization and nonspecific filtering were carried out. As described previously, absolute GSEA was carried out to investigate whether NF-κB target genes were differentially expressed between t(11;18) positive and translocation negative MALT lymphoma. The NF-κB target genes were collated from online data base (http://www.nf-kb.org), published works (http://bioinfo.lifl.fr/NF-KB, http://people.bu.edu/gilmore/nf-kb/target/index.html) and careful bioinformatic search (Table S1), and those that are transactivated by the non-canonical NF-κB pathway were identified according to previous investigations (11, 14-21). The significance of the GSEA results was assessed by statistical analyses (the nominal P value and False Discovery Rate). Leading edge analysis was further performed to identify the biologically important gene subset.

Tumor collection #2 includes 6 t(11;18)-positive and 8 t(11;18)-negative MALT lymphomas and the methods used for tissue sample collection, RNA isolation and reverse transcription have been described previously (22). Five micrograms of RNA were biotin-labeled and hybridized onto human oligonucleotide microarrays (Affymetrix HG-U133 Plus 2.0; Affymetrix, High Wycombe, UK). Data were analyzed using R/Bioconductor.

Statistical Analysis

Data are expressed as mean +/- SEM. Differences between groups were compared for significance using paired or unpaired 2-tailed Student's T tests, as appropriate, with the assistance of GraphPad InStat software. P values of less than 0.05 were considered statistically significant. See above sections and figure legends for statistical methods used to analyze gene expression in patient samples.

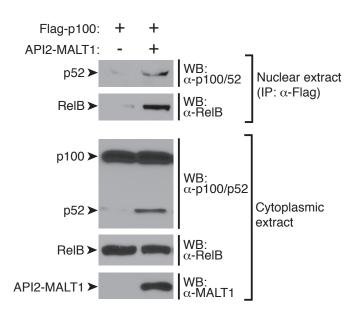
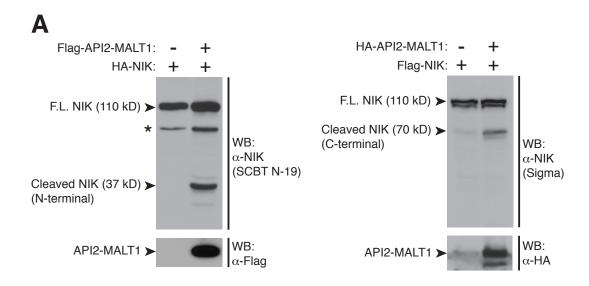


Fig. S1. API2-MALT1 expression results in the formation of p52/RelB dimers in the nucleus. HEK293T cells were transfected as indicated, and nuclear extracts were prepared. The ability of endogenous RelB to co-immunoprecipitate with nuclear p52 was assessed by Western blot. Data are representative of at least three separate experiments.



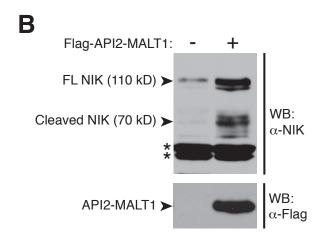


Fig. S2. API2-MALT1-dependent cleavage of NIK into 37 kD and 70 kD proteolytic fragments. (A) Additional antibodies confirm generation of N-terminal and C-terminal NIK fragments. Left panel: Western analysis using an antibody raised against the N-terminal portion of NIK and thereby recognizes only the 37 kD cleavage fragment. Right panel: Western analysis using an antibody raised against the C-terminal portion of NIK and thereby recognizes only the 70 kD cleavage fragment. (B) Cleavage of endogenous NIK by API2-MALT1. HEK293T cells were transfected with API2-MALT1, and endogenous NIK was detected by Western blot. Of note, we were able to detect endogenous NIK in HEK293T cells only when experiments were carried out in the presence of the proteasome inhibitor, MG132, consistent with the fact that NIK is highly unstable due to constitutive proteasomal degradation. Interestingly, in HEK293T cells treated with MG132, we observed that levels of endogenous NIK are enhanced upon expression of API2-MALT1. This implies that in addition to inducing NIK cleavage, expression of API2-MALT1 in these cells may also stimulate endogenous NIK production or enhance NIK stability via a mechanism other than inhibiting proteasome-dependent degradation. * = nonspecific band.

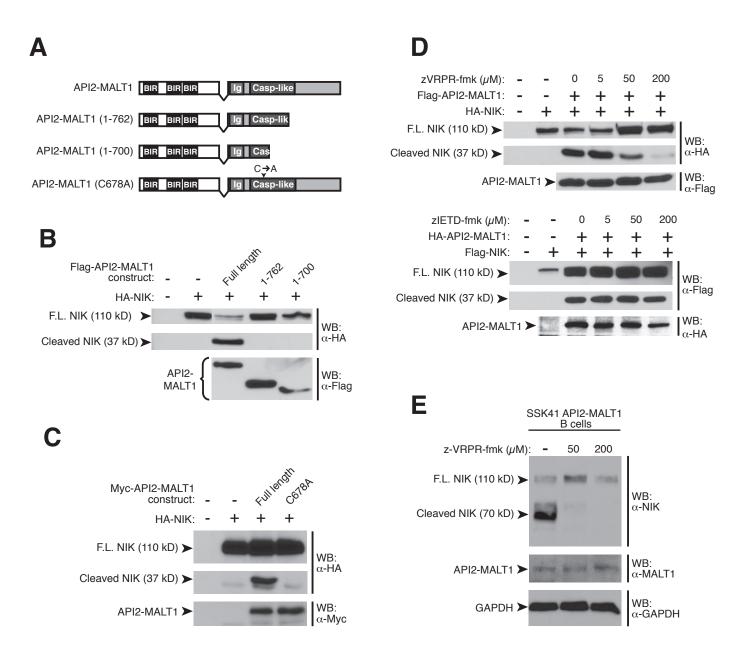


Fig. S3. Deletion, mutation, or inhibition of the MALT1 "caspase-like" domain results in loss of API2-MALT1-dependent NIK cleavage. (A) Schematic of API2-MALT1 mutants. (B) HEK293T cells were transfected with HA-NIK along with various Flag-tagged API2-MALT1 proteins as indicated. The 37 kD N-terminal NIK cleavage fragment was detected by Western blotting with α -HA. (C) HEK293T cells were transfected with either wild-type API2-MALT1 or API2-MALT1(C678A) mutant, along with HA-NIK as indicated. Western blot with α -HA was performed to detect full-length NIK and the 37 kD N-terminal NIK fragment. (D and E) HEK293T cells (D) or SSK41 cells (E) expressing API2-MALT1 were incubated with zVRPR-fmk or zIETD-fmk, and the NIK cleavage fragment was detected by Western blot. Data are representative of at least three separate experiments.

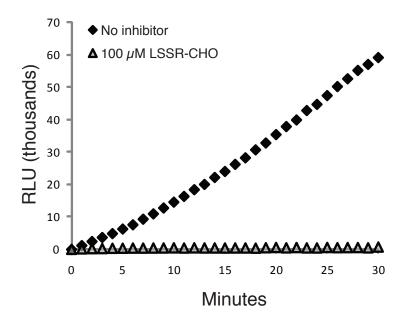
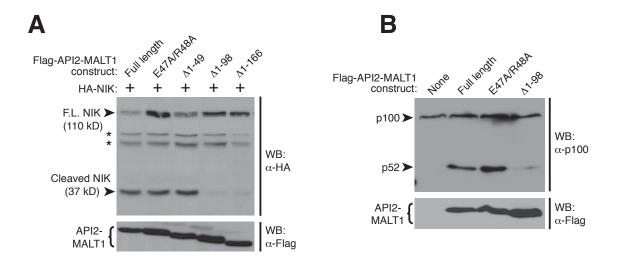


Fig. S4. *MALT1 protease activity assay.* Fluorescence release (RLU) due to Ac-LSSR-AMC substrate cleavage (100 μ M) in vitro by StrepII-tagged MALT1 (\spadesuit). Addition of Ac-LSSR-CHO (100 μ M) inhibits MALT1 proteolytic activity (Δ).



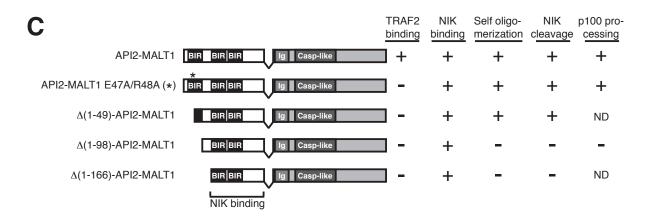


Fig. S5. The API2 moiety is required for association with and cleavage of NIK. (A) The API2-MALT1 auto-oligomerization domain, but not the TRAF2-binding domain, is required for NIK cleavage. HEK293T cells were transfected with HA-NIK, along with the indicated API2-MALT1 deletion mutants, and the generation of the 37 kD N-terminal NIK cleavage product was assessed by Western blotting with α -HA. Mutation or deletion of the previously identified TRAF2 binding site within BIR1 of the API2 moiety (E47A/R48A or Δ 1-49 mutants) does not prevent API2-MALT1-dependent NIK cleavage. In contrast, deletion of the C-terminal half of BIR1 (Δ 1-98), a region that mediates auto-oligomerization of API2-MALT1, does impede API2-MALT1-induced NIK cleavage. (B) API2-MALT1 mutants that lack the ability to bind and cleave NIK are unable to promote p100 processing to p52. HEK293T cells were transfected with the indicated API2-MALT1 mutants and processing of endogenous p100 was analyzed by Western blotting. (C) Schematic summary of the activities of various API2-MALT1 mutants. Results suggest that the API2 moiety of API2-MALT1 interacts with NIK via a site located C-terminal to the BIR1 domain (see Fig. 2F), and that API2 moiety-mediated auto-oligomerization is required to achieve efficient API2-MALT1-dependent NIK cleavage and p100 processing. ND= Not Determined.

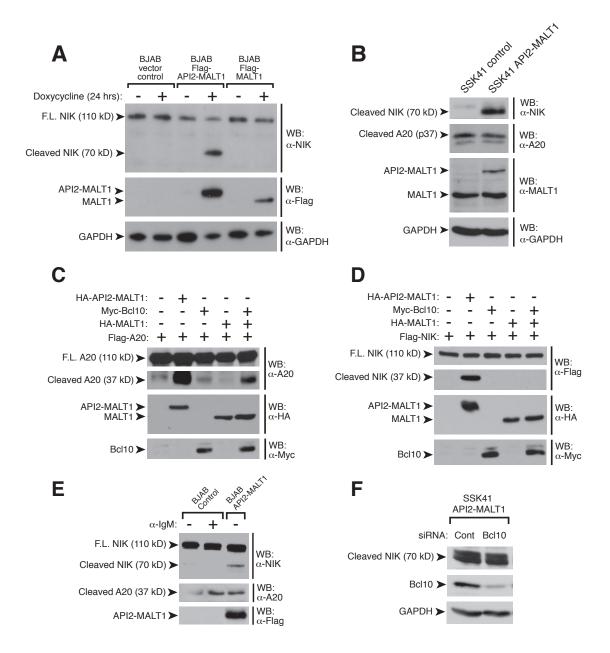


Fig. S6. Activation of wild-type MALT1 within the cell does not induce the cleavage of NIK. (A) BJAB B-cells expressing API2-MALT1 or MALT1 from a tetracycline inducible promotor were treated with or without doxycycline and analyzed for NIK cleavage by Western blot. (B) Unlike A20, NIK is not cleaved in SSK41 cells in the absence of API2-MALT1. Control cells or cells stably expressing API2-MALT1 were analyzed for the presence of the endogenous 70 kD C-terminal NIK cleavage fragment and 37 kD A20 C-terminal cleavage fragment by Western blot. (C and D) Co-expression of Bcl10 and MALT1 activates the MALT1 protease, but does not result in cleavage of NIK. HEK293T cells were transfected with A20 (C) or NIK (D), along with other indicated proteins, and the generation of the A20 (C) or NIK (D) cleavage product was assessed by Western blot. (E) B-cell receptor stimulation activates the MALT1 protease, but does not result in cleavage of NIK. Empty vector control or API2-MALT1-expressing BJAB cells were treated with or without anti-IgM as indicated, and the generation of endogenous cleaved NIK or A20 was detected by Western blot. (F) Bcl10 is not required for API2-MALT1-dependent NIK cleavage. API2-MALT1-expressing SSK41 cells were treated with control or Bcl10-specific siRNA. Bcl10 knock-down and NIK cleavage was then assessed by Western blot. Data are representative of at least three separate experiments.

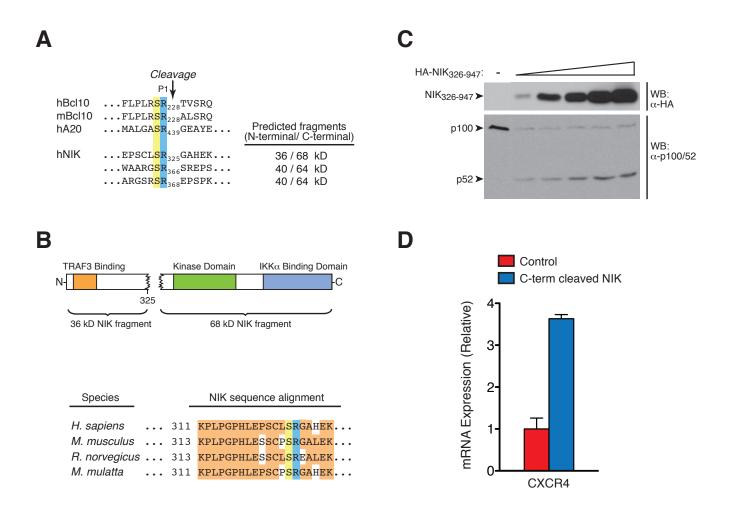


Fig. S7. The 70 kD C-terminal NIK cleavage fragment induces noncanonical NF-κB signaling. (A) Alignment of the MALT1 cleavage sites in Bcl10 and A20 with candidate sites for NIK cleavage. (B) Top-Schematic of API2-MALT1-dependent NIK cleavage. Bottom – The S324-R325 residues are conserved among species, suggesting that an evolutionarily relevant role for NIK cleavage at this site may exist. (C) The C-terminal NIK cleavage fragment induces concentration-dependent p100 processing. HEK293T cells were transfected with increasing concentrations of HA-NIK(326-947) expression plasmid and the resulting p100 processing was assessed by Western Blot. (D) The C-terminal NIK cleavage fragment induces the expression of CXCR4, a noncanonical NF-κB gene target (18). CXCR4 is a chemokine receptor that is implicated in B-lymphomagenesis (23, 24). We also found that CXCR4 is significantly upregulated in t(11;18)-positive MALT lymphomas (see Fig. 4F and G).

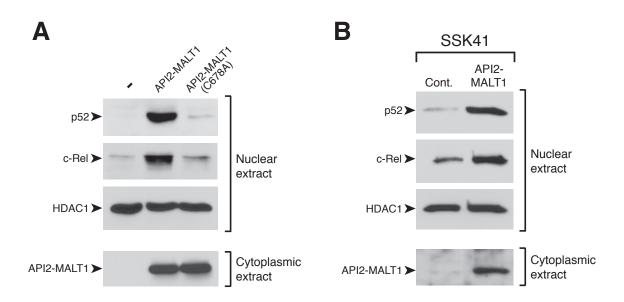


Fig. S8. *API2-MALT1 also induces c-Rel nuclear translocation.* Because previous work has shown that wild-type MALT1 signals to c-Rel upon BCR ligation (25), we also evaluated the effect of API2-MALT1 on c-Rel. (**A**) API2-MALT1 induces the nuclear translocation of c-Rel, and this requires an intact MALT1 protease domain. HEK293T cells were transfected as indicated, nuclear extracts were prepared, and the resulting nuclear translocation of p52 and c-Rel was assessed by Western blot. (**B**) API2-MALT1 expression in SSK41 cells is associated with enhanced nuclear translocation of p52 and c-Rel. Nuclear extracts were prepared for control and API2-MALT1 expressing SSK41 cells as indicated, and the levels of p52 and c-Rel were assessed by Western Blot.

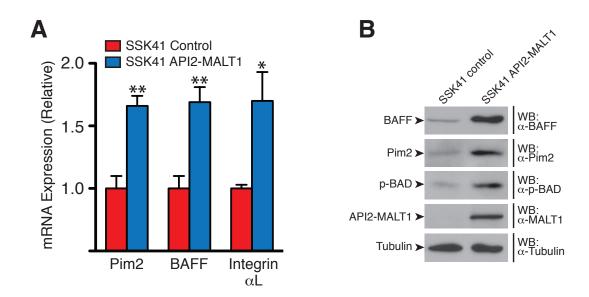


Fig. S9. *API2-MALT1 promotes noncanonical NF-κB target gene expression in SSK41 B-cells.* (A) Levels of mRNA transcript were analyzed by quantitative RT-PCR. Data are expressed as an average +/-SEM for at least three determinations. *= p< 0.05, **= p<0.005. (B) API2-MALT1 expression results in enhanced levels of BAFF, Pim-2 and phospho-Ser¹¹²-BAD. SSK41 cell lysates were prepared, and protein levels were compared by Western blotting.

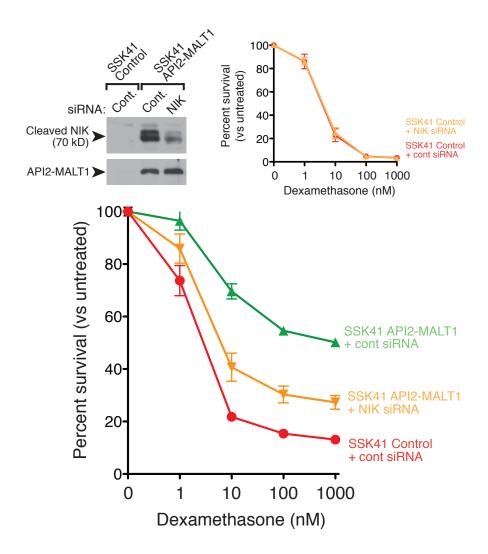


Fig. S10. *siRNA-mediated NIK knock-down abrogates API2-MALT1-dependent protection from dexamethasone-induced cell death.* Control or API2-MALT1 expressing SSK41 cells were transiently transfected with control or NIK siRNA and then treated with increasing concentrations of dexamethasone. The resulting cell viability was analyzed at 48 hours of dexamethasone treatment. Results are expressed as average ± SEM of three determinations. **Inserts** (*top left*): Western blotting demonstrates effective knock-down of the 70kD NIK cleavage fragment, (*top right*): NIK siRNA had no effect on the control SSK41 cells. Data are representative of at least three separate experiments.

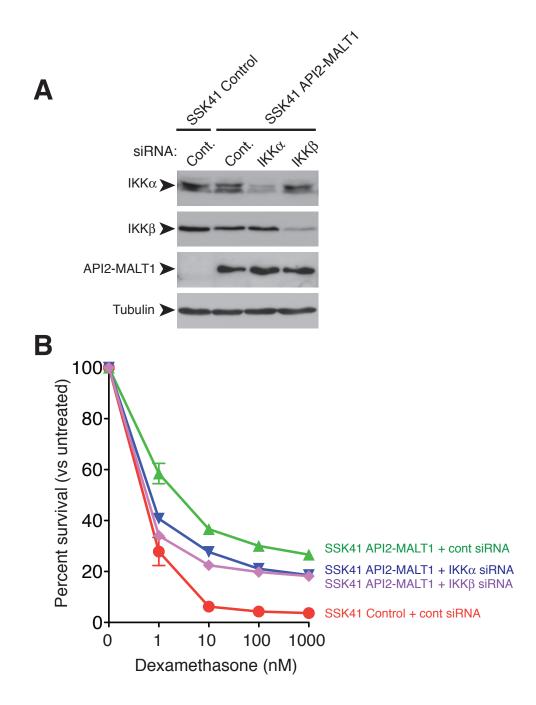


Fig. S11. API2-MALT1-dependent protection from dexamethasone-induced cell death is mediated by a combination of canonical and noncanonical NF-κB signaling. (A) Control or API2-MALT1 expressing SSK41 cells were transiently transfected with control, IKK α , or IKK β siRNA. Western blotting demonstrates effective and specific knock-down of the IKK subunits and confirms effective expression of API2-MALT1 in cells harboring the transgene. (B) Cells were then treated with increasing concentrations of dexamethasone. The resulting cell viability was analyzed after 48 hours of dexamethasone treatment. Results are expressed as average \pm SEM of three determinations, and are representative of three separate experiments.

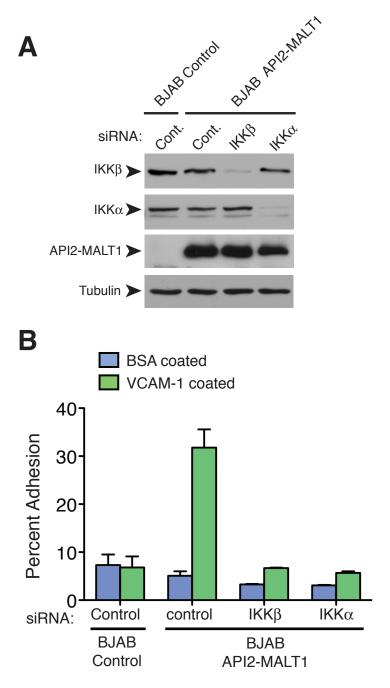


Fig. S12. Both canonical and noncanonical NF-κB signaling contribute to API2-MALT1-dependent adhesion. Control or API2-MALT1 expressing BJAB cells were transiently transfected with control, IKKβ, or IKKα siRNA. After 48 hours, cells were treated for 24 hours with doxycycline to induce API2-MALT1 expression in cells harboring the transgene, and were then plated onto either BSA- or VCAM-1 coated plates. (**A**) Western blotting demonstrates effective and specific knock-down of the IKK subunits as well as effective induction of API2-MALT1. (**B**) Following washing, the percentage of adherent cells was tallied.

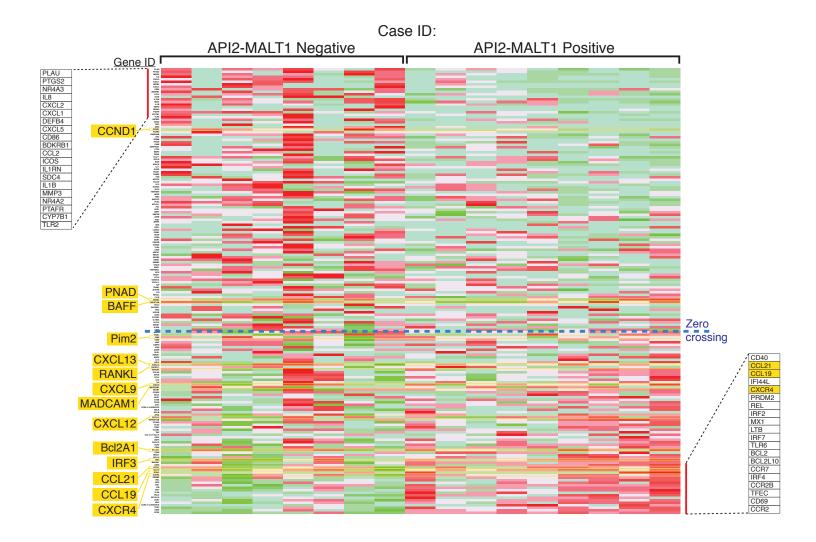


Fig. S13. Heat map illustration of gene expression in t(11;18)-positive vs. translocation negative MALT lymphomas from Collection #1 (See methods). Genes identified as noncanonical NF- κ B target genes are highlighted in yellow and labeled on the left. The top 20 leading edge core genes are shown.

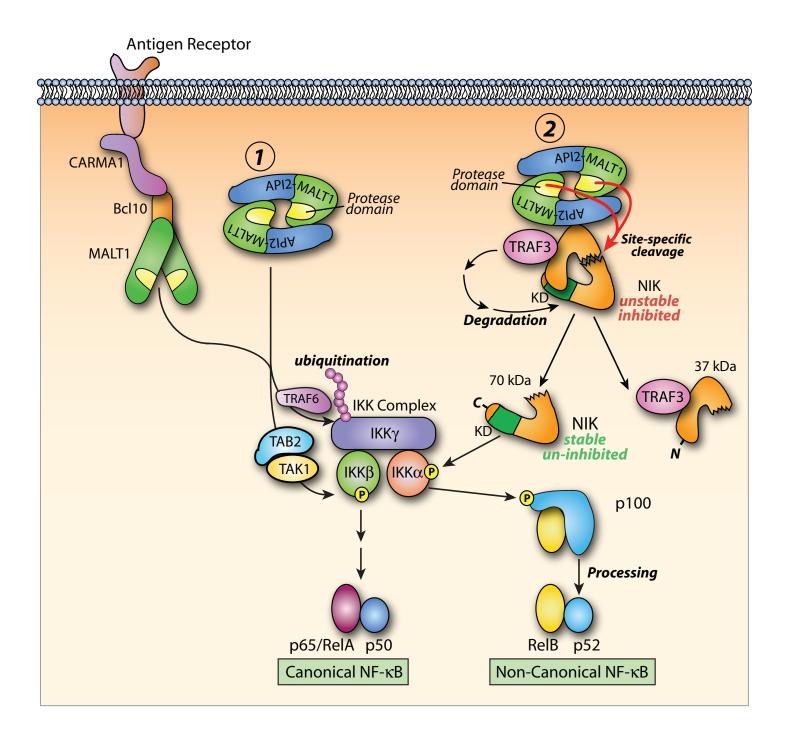


Fig. S14. Schematic illustrating our model for the role of NIK cleavage in API2-MALT1-dependent *lymphomagenesis.* We propose a model in which: (1) The API2 moiety mediates auto-oligomerization of API2-MALT1 and recruitment of NIK, (2) NIK is then placed in close proximity to the activated MALT1 protease domain and is made available as a substrate, (3) API2-MALT1-dependent NIK cleavage separates the TRAF3 binding site from the active kinase domain, and (4) The stabilized NIK kinase promotes deregulated noncanonical NF-κB signaling contributing to B-lymphomagenesis. The concept that the N-terminus of NIK contains an autoinhibitory domain that impairs NIK kinase activity (26), in addition to the TRAF3 binding site (27), is incorporated into the model.

Table S1.

Cono symbol	Cone full name	Course
Gene symbol PIM2	Gene full name Pim-2 oncogene	Source Immunity, 2006; 25: 403-415. Blood, 2008; 111(2): 750-760.
CCL21	chemokine (C-C motif) ligand 21 (Secondary lymphoid tissue chemokine, SLC)	Immunity, 2002; 17: 525-535. EMBO, 2004; 23: 4202-4210. J. Immunol., 2004; 173: 6161-6168. Immunity, 2002; 17: 525-535. EMBO, 2004; 23: 4202-4210. J. Immunol., 2004; 173: 6161-6168.
CCL19 CXCL13	chemokine (C-C motif) ligand 19 (Epstein Barr virus-induced molecule 1 ligand CC chemokine, ELC) chemokine (C-X-C motif) ligand 13 (B-lymphocyte chemoattractant, BLC)	Immunity, 2002; 17: 525-535. EMBO, 2004; 23: 4202-4210. J. Immunol., 2004; 173: 6161-6168.
TNFSF13B CXCL12	B-cell activating factor belonging to the TNF family (BAFF) chemokine (C-X-C motif) ligand 12 (stromal derived factor-lalpha, SDF-1)	Immunity, 2002; 17: 525-535. EMBO, 2004; 23, 4202-4210. Immunity, 2002; 17: 525-535. EMBO, 2004; 23, 4202-4210.
BCL2A1	BCL2-related protein A1	Immunity, 2006; 25: 403-415.
CXCR4 TNFSF11	chemokine (C-S-C motif) receptor 4 tumor necrosis factor (ligand) superfamily, member 11 (RANK-L)	PNAS, 2004; 101: 141-146. Science, 2001; 293: 1495-1499.
CCND1	Cyclin D1	Endocrinology, 2007; 148(1): 268-278.
CXCL9 NTAN1	chemokine (C-X-C) ligand 9 N-terminal asparagine amidase (PNAD)	PNAS, 2004; 101: 141-146. J. Immunol., 2004: 173: 6161-6168.
MADCAM1	mucosal vascular addressin cell adhesion molecule 1	Blood, 2007; 110: 2381-2389.
IRF3 TRIP10	interferon regulatory factor 3 thyroid hormone receptor interactor 10	EMBO, 2004; 23 : 4202-4210. bioinformatics
IL32	interleukin 32	bioinformatics
RCP9 ANKRD1	calcitonin gene-related peptide-receptor component protein ankyrin repeat domain 1 (cardiac muscle)	bioinformatics bioinformatics
TNFRSF10B	tumor necrosis factor receptor superfamily, member 10b	bioinformatics
AKR1C2 LDHB	aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2 lactate dehydrogenase B	bioinformatics bioinformatics
TEAD1	TEA domain family member 1 (SV40 transcriptional enhancer factor)	bioinformatics
PRDM2 BACE2	PR domain containing 2, with ZNF domain beta-site APP-cleaving enzyme 2	bioinformatics bioinformatics
SUV39H1	suppressor of variegation 3-9 homolog 1 (Drosophila)	bioinformatics
IL1F9 ALOX12B	interleukin 1 family, member 9 arachidonate 12-lipoxygenase, 12R type	bioinformatics bioinformatics
CARD15	caspase recruitment domain family, member 15	bioinformatics
CD74 CXCL2	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated) chemokine (C-X-C motif) ligand 2	bioinformatics bioinformatics
DEFB4	defensin, beta 4	bioinformatics
IL15RA TPMT	interleukin 15 receptor, alpha thiopurine S-methyltransferase	bioinformatics bioinformatics
TLR6 TLR4	toll-like receptor 6 toll-like receptor 4	bioinformatics bioinformatics
SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	bioinformatics bioinformatics
PLA2G2E	phospholipase A2, group IIE	bioinformatics
ADAMTS12 CSF2RA	ADAM metallopeptidase with thrombospondin type 1 motif, 12 colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	bioinformatics bioinformatics
MMP8 CCL7	matrix metallopeptidase 8 (neutrophil collagenase)	bioinformatics bioinformatics
TNFRSF21	chemokine (C-C motif) ligand 7 tumor necrosis factor receptor superfamily, member 21	bioinformatics bioinformatics
PLA2G4A	phospholipase A2, group IVA (cytosolic, calcium-dependent)	bioinformatics
LAMC2 BCL2L10	laminin, gamma 2 BCL2-like 10 (apoptosis facilitator)	bioinformatics bioinformatics
TNFSF6 CD105	tumor necrosis factor superfamily, member 6	bioinformatics
TNFRSF6	homodimeric transmembrane protein which is a major glycoprotein of the vascular endothelium tumor necrosis factor receptor superfamily, member 6, decoy	bioinformatics bioinformatics
TNFSF5 BM2	tumor necrosis factor superfamily, member 5 influenza B virus BM2	bioinformatics bioinformatics
HC3	proteasome subunit HC3	bioinformatics
SIAT8A TBR	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 1 tuberin	bioinformatics bioinformatics
TNFRSF5	tumor necrosis factor receptor superfamily, member 5, decoy	bioinformatics
RBCK1 CCR2A	RanBP-type and C3HC4-type zinc finger containing 1	bioinformatics
CCR2B	chemokine (C-C motif) receptor 2 isoform A chemokine (C-C motif) receptor 2 isoform B	bioinformatics bioinformatics
BIRC2 ICAM1	baculoviral IAP repeat-containing 2	Blood, 2005; 106(4): 1392 - 1399 Blood, 2005; 106(4): 1392 - 1399
CX3CL1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor chemokine (C-X3-C motif) ligand 1	Blood, 2005; 106(4): 1392 - 1399
NR4A3 BCL10	nuclear receptor subfamily 4, group A, member 3 B-cell CLL/lymphoma 10	Journal of Biological Chemistry, 2005 ; 280(32) : 29256-29262 Journal of Biological Chemistry, 2006 ; 281(1) : 167 - 175
LMP2	low molecular weight protein 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
CTSL1 KLK3	cathepsin L1 kallikrein-related peptidase 3	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
BMP2	bone morphogenetic protein 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
AMH NOD2	anti-Mullerian hormone nucleotide-binding oligomerization domain containing 2	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CYP2C11	Cytochrome P450 2C11	http://people.bu.edu/gilmore/nf-kb/target/index.html
NK4 CCL15	N-terminal hairpin and subsequent four-kringle domains of hepatocyte growth factor chemokine (C-C motif) ligand 15	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	http://people.bu.edu/gilmore/nf-kb/target/index.html
IL1B TERT	interleukin 1, beta telomerase reverse transcriptase	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
SELP	selectin P (granule membrane protein 140kDa, antigen CD62)	http://people.bu.edu/gilmore/nf-kb/target/index.html
TNFAIP3 CD44	tumor necrosis factor, alpha-induced protein 3 CD44 antigen (homing function and Indian blood group system)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
NOS2A	nitric oxide synthase 2A (inducible, hepatocytes)	http://people.bu.edu/gilmore/nf-kb/target/index.html
SOD2 CSF3	superoxide dismutase 2, mitochondrial colony stimulating factor 3 (granulocyte)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
BCL3	B-cell CLL/lymphoma 3	http://people.bu.edu/gilmore/nf-kb/target/index.html
RAGE GRIN1	renal tumor antigen glutamate receptor, ionotropic, N-methyl D-aspartate 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IGHG4	immunoglobulin heavy constant gamma 4 (G4m marker)	http://people.bu.edu/gilmore/nf-kb/target/index.html
IGHG3 SERPINA1	immunoglobulin heavy constant gamma 3 (G3m marker) serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
NR4A2	nuclear receptor subfamily 4, group A, member 2 nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	http://people.bu.edw/gilmore/nf-kb/target/index.html http://people.bu.edw/gilmore/nf-kb/target/index.html
NFKB1 NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	http://people.bu.edu/gilmore/nf-kb/target/index.html
BCL2A1 ADH1A	BCL2-related protein A1 alcohol dehydrogenase 1A (class I), alpha polypeptide	http://people.bu.edw/gilmore/nf-kb/target/index.html http://people.bu.edw/gilmore/nf-kb/target/index.html
AGER	advanced glycosylation end product-specific receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html
AMH	anti-Mullerian hormone ADP-ribosylation factor related protein 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ARFRP1 BCL2L1	BCL2-like 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
BDKRB1 BLR1	bradykinin receptor B1	http://people.bu.edu/gilmore/nf-kb/target/index.html
BMP2	Burkitt lymphoma receptor 1, GTP binding protein (chemokine (C-X-C motif) receptor 5) bone morphogenetic protein 2	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CASP4 CD209	caspase 4, apoptosis-related cysteine peptidase CD209 antigen	http://people.bu.edw/gilmore/nf-kb/target/index.html http://people.bu.edw/gilmore/nf-kb/target/index.html
CRP	C-reactive protein, pentraxin-related	http://people.bu.edu/gilmore/nf-kb/target/index.html
CXCL10 CXCL9	chemokine (C-X-C motif) ligand 10 chemokine (C-X-C motif) ligand 9	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
FTH1	ferritin, heavy polypeptide 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
GSTP1 HMOX1	glutathione S-transferase pi	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IER3	heme oxygenase (decycling) 1 immediate early response 3	http://people.bu.edu/gilmore/nf-kb/target/index.html
IFNB1	interferon, beta 1, fibroblast	http://people.bu.edu/gilmore/nf-kb/target/index.html
IL1RN KLK3	interleukin 1 receptor antagonist kallikrein 3, (prostate specific antigen)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
NPY1R NQO1	neuropeptide Y receptor Y1	http://people.bu.edw/gilmore/nf-kb/target/index.html http://people.bu.edw/gilmore/nf-kb/target/index.html
OPRM1	NAD(P)H dehydrogenase, quinone 1 opioid receptor, mu 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
PLAU	plasminogen activator, urokinase	http://people.bu.edu/gilmore/nf-kb/target/index.html
PLCD1 PTAFR	phospholipase C, delta 1 platelet-activating factor receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PTGDS	prostaglandin D2 synthase 21kDa (brain)	http://people.bu.edu/gilmore/nf-kb/target/index.html
PTGS2 SCNN1A	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) sodium channel, nonvoltage-gated 1 alpha	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
SELE	selectin E (endothelial adhesion molecule 1)	http://people.bu.edu/gilmore/nf-kb/target/index.html
TACR1 TAP1	tachykinin receptor 1 transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
TFPI2 TNC	Tissue factor pathway inhibitor 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
TNF	tenascin C (hexabrachion) tumor necrosis factor (TNF superfamily, member 2)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html

TNFRSF9 VEGF	tumor necrosis factor receptor superfamily, member 9	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CCL5	vascuai enoquenai giovai nacioi chemokine (C-C motif) ligand 5	http://people.bu.edu/gilmore/nf-kb/target/index.html
CYP2E1	cytochrome P450, family 2, subfamily E, polypeptide 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
PGK1 CTSB	phosphoglycerate kinase 1 cathepsin B	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
HMGN1	high-mobility group nucleosome binding domain 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
CCND2 BGN	cyclin D2 biglycan	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ENO2	enolase 2 (gamma, neuronal)	http://people.bu.edu/gilmore/nf-kb/target/index.html
VIM JUNB	vimentin	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ELF3	jun B proto-oncogene E74-like factor 3 (ets domain transcription factor, epithelial-specific)	http://people.bu.edu/gilmore/nf-kb/target/index.html
EGR1	early growth response 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
CCND3 TP53	evelin D3 tumor protein p53 (Li-Fraumeni syndrome)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ENG	endoglin (Osler-Rendu-Weber syndrome 1)	http://people.bu.edu/gilmore/nf-kb/target/index.html
BNIP3 EGFR	BCL2/adenovirus E1B 19kDa interacting protein 3 epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
SDC4	Syndecian 4 (amphiglycan, ryudocan)	http://people.bu.edu/gilmore/nf-kb/target/index.html
IER2 MX1	immediate early response 2 myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse)	http://people.bu.edu/gilmore/nf-kb/target/index.html
GBP1	guanylate binding protein 1, interferon-inducible protein p/8 (mouse)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
KLF10	Kruppel-like factor 10	http://people.bu.edu/gilmore/nf-kb/target/index.html
IRF1 IGFBP2	interferon regulatory factor 1 insulin-like growth factor binding protein 2, 36kDa	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IL8	interleukin 8	http://people.bu.edu/gilmore/nf-kb/target/index.html
GCLC SOX9	glutamate-cysteine ligase, catalytic subunit SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
STAT5A	signal transducer and activator of transcription 5A	http://people.bu.edu/gilmore/nf-kb/target/index.html
THBS2	thrombospondin 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
UBE2M UPP1	ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast) uridine phosphorylase 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IRF2	interferon regulatory factor 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
APOE ABCA1	apolipoprotein E ATP-binding cassette, sub-family A (ABC1), member 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
BCL2	B-cell CLL/lymphoma 2	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
DIO2	deiodinase, iodothyronine, type II	http://people.bu.edu/gilmore/nf-kb/target/index.html
VCAM1 GCLM	vascular cell adhesion molecule 1 glutamate-cysteine ligase, modifier subunit	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
MMP9	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	http://people.bu.edu/gilmore/nf-kb/target/index.html
CD48 PDGFB	CD48 antigen (B-cell membrane protein) platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
TRAF2	TNF receptor-associated factor 2	http://people.bu.edu/gilmore/nf-kb/target/index.html
IFI44L	interferon-induced protein 44-like	http://people.bu.edu/gilmore/nf-kb/target/index.html
CD83 CXCL1	CD83 antigen (activated B lymphocytes, immunoglobulin superfamily) chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IRF4	interferon regulatory factor 4	http://people.bu.edu/gilmore/nf-kb/target/index.html
TFF3 MUC2	trefoil factor 3 (intestinal) mucin 2, intestinal/tracheal	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
AFP	alpha-fetoprotein	http://people.bu.edu/gilmore/nf-kb/target/index.html
FAS	Fas (TNF receptor superfamily, member 6)	http://people.bu.edu/gilmore/nf-kb/target/index.html
UGCG TLR2	UDP-glucose ceramide glucosyltransferase toll-like receptor 2	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PLK3	polo-like kinase 3 (Drosophila)	http://people.bu.edu/gilmore/nf-kb/target/index.html
CD40 RELB	CD40 antigen (TNF receptor superfamily member 5) v-rel reticuloendotheliosis viral oncogene homolog B, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3 (avian)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IL6	interleukin 6 (interferon, beta 2)	http://people.bu.edu/gilmore/nf-kb/target/index.html
GAD1 IGFBP1	glutamate decarboxylase 1 (brain, 67kDa) insulin-like growth factor binding protein 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PRL	prolactin	http://people.bu.edu/gilmore/nf-kb/target/index.html
TRAF1	TNF receptor-associated factor 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
CD86 CD38	CD86 antigen (CD28 antigen ligand 2, B7-2 antigen) CD38 antigen (p45)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
POMC	proopiomelanocortin (adrenocorticotropin/ beta-lipotropin/ alpha-melanocyte stimulating hormone/ beta-melanocyte stimulating hormone/ beta-endorphin)	http://people.bu.edu/gilmore/nf-kb/target/index.html
APOC3 MMP3	apolipoprotein C-III matrix metallopeptidase 3 (stromelysin 1, progelatinase)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IL15	interfection 15	http://people.bu.edu/gilmore/nf-kb/target/index.html
WT1 PTX3	Wilms tumor 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
APOBEC2	pentraxin-related gene, rapidly induced by IL-1 beta apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 2	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
MAP4K1	mitogen-activated protein kinase kinase kinase lase 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
CCR7 IL2RA	chemokine (C-C motif) receptor 7 interleukin 2 receptor, alpha	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CDX1	caudal type homeo box transcription factor 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
RAG1	recombination activating gene 1	http://people.bu.edu/gilmore/nf-kb/target/index.html
P11 TFEC	26 serine protease transcription factor EC	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
FCER2	Fe fragment of IgE, low affinity II, receptor for (CD23A)	http://people.bu.edu/gilmore/nf-kb/target/index.html
MTHFR PDYN	5,10-methylenetetrahydrofolate reductase (NADPH) prodynorphin	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CD3G	CD3G antigen, gamma polypeptide (TiT3 complex)	http://people.bu.edu/gilmore/nf-kb/target/index.html
OXTR	oxylocin receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html
IL11 LTA	lymphotoxin alpha (TNF superfamily, member 1)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CCR5	chemokine (C-C motif) receptor 5	http://people.bu.edu/gilmore/nf-kb/target/index.html
GIF CSF1	gastric intrinsic factor (vitamin B synthesis) colony stimulating factor 1 (macrophage)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	http://people.bu.edu/gilmore/nf-kb/target/index.html
CD80 TNIP1	CD80 antigen (CD28 antigen ligand 1, B7-1 antigen) TNFAIP3 interacting protein 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
EPO	erythropoietin	http://people.bu.edu/gilmore/nf-kb/target/index.html
LTB CYP7B1	lymphotoxin beta (TNF superfamily, member 3) cytochrome P450, family 7, subfamily B, polypeptide 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
IL10	interleukin 10	http://people.bu.edu/gilmore/nf-kb/target/index.html
NFKB2	nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100)	http://people.bu.edu/gilmore/nf-kb/target/index.html
IL13 IL2	interleukin 13	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CXCL5	chemokine (C-X-C motif) ligand 5	http://people.bu.edu/gilmore/nf-kb/target/index.html
CCL22 MADCAM1	chemokine (C-C motif) ligand 22	http://people.bu.edu/gilmore/nf-kb/target/index.html
MADCAM1 REV3L	mucosal vascular addressin cell adhesion molecule 1 REV3-like, catalytic subunit of DNA polymerase zeta (yeast)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PTGIS	prostaglandin 12 (prostacyclin) synthase	http://people.bu.edu/gilmore/nf-kb/target/index.html
IL9 IL1A	interleukin 9 interleukin 1, alpha	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PGR	progesterone receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html
IRF7 FGF8	interferon regulatory factor 7 fibroblast growth factor 8 (androgen-induced)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
BAX	BCL2-associated X protein	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ABCC6	ATP-binding cassette, sub-family C (CFTR/MRP), member 6	http://people.bu.edu/gilmore/nf-kb/target/index.html
SERPINA2 CCND1	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 2 cyclin D1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
TAPBP	TAP binding protein (tapasin)	http://people.bu.edu/gilmore/nf-kb/target/index.html
LGALS3 UCP2	lectin, galactoside-binding, soluble, 3 (galectin 3) uncoupling protein 2 (mitochondrial, proton carrier)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
PIM1	pim-1 oncogene	http://people.bu.edu/gilmore/nf-kb/target/index.html
GADD45B	growth arrest and DNA-damage-inducible, beta	http://people.bu.edu/gilmore/nf-kb/target/index.html
RIPK2 ADAM19	receptor-interacting serine-threonine kinase 2 ADAM metallopeptidase domain 19 (meltrin beta)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CD69	CD69 antigen (p60, early T-cell activation antigen)	http://people.bu.edu/gilmore/nf-kb/target/index.html
HGF ABCB1	hepatocyte growth factor (hepapoietin A; scatter factor) ATP-binding cassette, sub-family B (MDR/TAP), member 1	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
UPK1B	uroplakin 1B	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
CCL11	chemokine (C-C motif) ligand 11	http://people.bu.edu/gilmore/nf-kb/target/index.html
CXCL11 GZMB	chemokine (C-X-C motif) ligand 11 granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
XDH	xanthine dehydrogenase	http://people.bu.edu/gilmore/nf-kb/target/index.html
IFNG	interferon, gamma inducible T-cell co-stimulator	http://people.bu.edu/gilmore/nf-kb/target/index.html http://people.bu.edu/gilmore/nf-kb/target/index.html
ICOS		

FN1	fibronectin 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
ERBB2	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
KITLG	KIT ligand	http://people.bu.edu/gilmore/nf-kb/target/index.html			
FASLG	Fas ligand (TNF superfamily, member 6)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
HLA-G	HLA-G histocompatibility antigen, class I, G	http://people.bu.edu/gilmore/nf-kb/target/index.html			
TGM2	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
NR3C1	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
PENK	proenkephalin	http://people.bu.edu/gilmore/nf-kb/target/index.html			
PAX8	paired box gene 8	http://people.bu.edu/gilmore/nf-kb/target/index.html			
CCL2	chemokine (C-C motif) ligand 2	http://people.bu.edu/gilmore/nf-kb/target/index.html			
S100A6	S100 calcium binding protein A6 (calcyclin)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
EDN1	endothelin 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
HPSE	heparanase	http://people.bu.edu/gilmore/nf-kb/target/index.html			
SNAI1	snail homolog 1 (Drosophila)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
KCNK5	potassium channel, subfamily K, member 5	http://people.bu.edu/gilmore/nf-kb/target/index.html			
ABCG5	ATP-binding cassette, sub-family G (WHITE), member 5 (sterolin 1)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
F11R	F11 receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html			
G6PD	glucose-6-phosphate dehydrogenase	http://people.bu.edu/gilmore/nf-kb/target/index.html			
ORM1	orosomucoid 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
ADORA1	adenosine A1 receptor	http://people.bu.edu/gilmore/nf-kb/target/index.html			
C4BPA	complement component 4 binding protein, alpha	http://people.bu.edu/gilmore/nf-kb/target/index.html			
HAS1	hyaluronan synthase 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
REL	v-rel reticuloendotheliosis viral oncogene homolog (avian)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
CCL3	chemokine (C-C motif) ligand 3	http://people.bu.edu/gilmore/nf-kb/target/index.html			
CCL4	chemokine (C-C motif) ligand 4	http://people.bu.edu/gilmore/nf-kb/target/index.html			
CFLAR	CASP8 and FADD-like apoptosis regulator	http://people.bu.edu/gilmore/nf-kb/target/index.html			
PRF1	perforin 1 (pore forming protein)	http://people.bu.edu/gilmore/nf-kb/target/index.html			
HBE1	hemoglobin, epsilon 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
C4A	complement component 4A	http://people.bu.edu/gilmore/nf-kb/target/index.html			
OLR1	oxidised low density lipoprotein (lectin-like) receptor 1	http://people.bu.edu/gilmore/nf-kb/target/index.html			
AGT	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	http://people.bu.edu/gilmore/nf-kb/target/index.html			

Table S2.

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BNIP3

Leading edge core set of NF-kB target genes, which are differentially enriched in MALT lymphoma with t(11;18) vs. no translocation Enrichment Gene Description Chromosome Entrez II Signal to Band noise ratio Score Expression of genes enriched in translocation negative MALT lymphoma PLAU 10q24 5328 0.759 0.018 1 plasminogen activator, urokinase 2 PTGS2 prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase 1q25.2-q25.3 5743 0.714 0.034 3 NR4A3 0.050 nuclear receptor subfamily 4, group A, member 3 9q22 8013 0.687 4 IL8 interleukin 8 3576 0.670 0.065 4q13-q21 5 CXCL2 chemokine (C-X-C motif) ligand 2 4q21 2920 0.658 0.080 2919 6 CXCL1 chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating a 4q21 0.597 0.092 7 DEFB4 defensin, beta 4 8p23.1-p22 1673 0.562 0.104 8 CXCL5 6374 chemokine (C-X-C motif) ligand 5 0.527 0.113 4q12-q13 9 CD86 CD86 molecule 942 0.497 0.120 3q21 10 BDKRB1 bradykinin receptor B1 14q32.1-q32.2 623 0.475 0.127 11 CCL2 chemokine (C-C motif) ligand 2 17q11.2-q12 6347 0.469 0.137 12 ICOS inducible T-cell co-stimulator 2q33 29851 0.455 0.145 0.155 13 IL1RN interleukin 1 receptor antagonist 2q14.2 3557 0.451 14 SDC4 svndecan 4 20q12 6385 0.448 0.165 15 IL1B interleukin 1, beta 3553 0.433 0.172 2q14 16 MMP3 matrix metallopeptidase 3 (stromelysin 1, progelatinase) 11q22.3 4314 0.416 0.176 4929 0.401 17 NR4A2 nuclear receptor subfamily 4, group A, member 2 2q22-q23 0.180 platelet-activating factor receptor 18 **PTAFR** 1p35-p34.3 5724 0.393 0.185 19 cytochrome P450, family 7, subfamily B, polypeptide 1 8q21.3 9420 0.393 0.194 CYP7B1 20 TLR2 toll-like receptor 2 4q32 7097 0.384 0.198 21 IGFBP2 insulin-like growth factor binding protein 2, 36kDa 2q33-q34 3485 0.379 0.206 22 SOD2 superoxide dismutase 2, mitochondrial 6q25.3 6648 0.376 0.213 7033 0.222 23 TFF3 trefoil factor 3 (intestinal) 21q22.3 0.376 24 DIO2 deiodinase, iodothyronine, type II 14q24.2-q24.3 1734 0.366 0.226 25 0.364 0.233 cyclin D1 11q13 595 CCND1 26 FCER2 Fc fragment of IgE, low affinity II, receptor for (CD23) 19p13.3 2208 0.362 0.240 27 GADD45B growth arrest and DNA-damage-inducible, beta 19p13.3 4616 0.354 0.244 0.251 28 TNC 9q33 3371 0.351 0.259 29 GZMB 3002 0.351 granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine 14q11.2 PTGIS 5740 0.344 0.264 30 prostaglandin I2 (prostacyclin) synthase 20q13.13 31 PAX8 paired box 8 2q12-q14 7849 0.324 0.258 32 SERPINA1 serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitryps 14q32.1 5265 0.322 0.264 33 5806 PTX3 pentraxin-related gene, rapidly induced by IL-1 beta 3q25 0.321 0.271 BMP2 bone morphogenetic protein 2 0.306 0.268 34 20p12 650 35 PENK proenkephalin 8q23-q24 5179 0.305 0.274 36 CCL11 chemokine (C-C motif) ligand 11 17q21.1-q21.2 6356 0.291 0.269 37 KITLG 4254 0.29 0.274 KIT ligand 12q22 biglycan 0.288 0.278 38 BGN Xq28 633 39 ADH1A alcohol dehydrogenase 1A (class I), alpha polypeptide 4q21-q23 124 0.275 0.273 3589 40 IL11 19q13.3-q13.4 0.272 0.276 41 EGFR epidermal growth factor receptor (erythroblastic leukemia viral (v-e 7p12 1956 0.272 0.282 42 7003 TEAD1 TEA domain family member 1 (SV40 transcriptional enhancer facted 11p15.2 0.272 0.288 43 THBS2 thrombospondin 2 7058 0.266 0.289 6q27 0.264 0.294 44 FAS Fas (TNF receptor superfamily, member 6) 10q24.1 355 45 APOC3 apolipoprotein C-III 11q23.1-q23.2 345 0.247 0.279 46 CCL22 chemokine (C-C motif) ligand 22 16q13 6367 0.245 0.284 47 0.239 0.282 IL13 interleukin 13 5q31 3596 48 KCNK5 potassium channel, subfamily K, member 5 6p21 8645 0.237 0.286 49 ELF3 E74-like factor 3 (ets domain transcription factor, epithelial-specific 1q32.2 1999 0.23 0.282 50 3604 0.229 TNFRSF9 tumor necrosis factor receptor superfamily, member 9 1p36 0.286 51 HPSE 10855 0.228 0.29 heparanase 4q21.3 52 IER3 6p21.3 8870 0.224 0.292 immediate early response 3 53 AKR1C2 aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogena 10p15-p14 1646 0.224 0.298 54 PLK3 polo-like kinase 3 (Drosophila) 1p34.1 1263 0.22 0.298 BCL2L1 BCL2-like 1 0.295 55 20q11.21 598 0.214 56 FN1 2q34 2335 0.212 0.298 fibronectin 1 57 UPP1 7p12.3 7378 0.21 0.299 uridine phosphorylase 1 58 GBP1 guanylate binding protein 1, interferon-inducible, 67kDa 1p22.2 2633 0.208 0.302 59 UBE2M 9040 0.205 0.302 ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast) 19a13.43 60 IUNB iun B proto-oncogene 19p13.2 3726 0.203 0.304 61 PIM1 6p21.2 5292 0.203 0.309 pim-1 oncogene

10q26.3

664

0.201

0.312

BCL2/adenovirus E1B 19kDa interacting protein 3

		ned in translocation positive MALT lymphoma		105-0	0.055	
94	TNFSF13B	tumor necrosis factor (ligand) superfamily, member 13b	13q32-q34	10673	0.066	0.208
95	BCL3	B-cell CLL/lymphoma 3	19q13.1-q13.2	602	0.064	0.205
96	SUV39H1	suppressor of variegation 3-9 homolog 1 (Drosophila)	Xp11.23	6839	0.062	0.204
97	TP53	tumor protein p53	17p13.1	7157	0.045	0.175
98	UPK1B	uroplakin 1B	3q13.3-q21	7348	0.040	0.169
99	BACE2	beta-site APP-cleaving enzyme 2	21q22.3	25825	0.030	0.150
100	CYP2E1	cytochrome P450, family 2, subfamily E, polypeptide 1	10q24.3-qter	1571	0.027	0.147
101	IL15RA	interleukin 15 receptor, alpha	10p15-p14	3601	0.027	0.147
102	KLF10	Kruppel-like factor 10	8q22.2	7071	0.026	0.146
103	ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1	7q21.12	5243	0.021	0.139
104	IL2RA	interleukin 2 receptor, alpha	10p15-p14	3559	0.013	0.125
105	CD83	CD83 molecule	6p23	9308	0.006	0.112
106	MMP9	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa t	· · · · · · · · · · · · · · · · · · ·	4318	-0.011	0.082
107	PGK1	phosphoglycerate kinase 1	Xq13	5230	-0.013	0.079
108	PIM2	pim-2 oncogene	Xp11.23	11040	-0.015	0.077
109	CD80	CD80 molecule	3q13.3-q21	941	-0.016	0.076
110	BAX	BCL2-associated X protein	19q13.3-q13.4	581	-0.019	0.071
111	C4BPA	complement component 4 binding protein, alpha	1q32	722	-0.020	0.069
112	ENG	endoglin	9q33-q34.1	2022	-0.023	0.066
113	AGER	advanced glycosylation end product-specific receptor	6p21.3	177	-0.027	0.0593
114	OLR1	oxidized low density lipoprotein (lectin-like) receptor 1	12p13.2-p12.3	4973	-0.0325	0.0499
115	HMOX1	heme oxygenase (decycling) 1	22q12	3162	-0.0349	0.0477
116	ENO2	enolase 2 (gamma, neuronal)	12p13	2026	-0.0369	0.0447
117	IL15	interleukin 15	4q31	3600	-0.0438	0.0351
118	SELP	selectin P (granule membrane protein 140kDa, antigen CD62)	1q22-q25	6403	-0.0479	0.0293
119	CXCL13	chemokine (C-X-C motif) ligand 13	4q21	10563	-0.0497	0.0271
120	TNFSF11	tumor necrosis factor (ligand) superfamily, member 11	13q14	8600	-0.0521	0.0243
121	TNFAIP3	tumor necrosis factor, alpha-induced protein 3	6q23	7128	-0.0572	0.0185
122	CFLAR	CASP8 and FADD-like apoptosis regulator	2q33-q34	8837	-0.0588	0.018
123	APOE	apolipoprotein E	19q13.2	348	-0.0591	0.0187
124	CCL5	chemokine (C-C motif) ligand 5	17q11.2-q12	6352	-0.0606	0.0175
125	IL32	interleukin 32	16p13.3	9235	-0.0716	0.000704
126	IL6	interleukin 6 (interferon, beta 2)	7p21	3569	-0.0733	-0.000587
127	CXCL9	chemokine (C-X-C motif) ligand 9	4q21	4283	-0.0835	-0.0169
128	MADCAM1	mucosal vascular addressin cell adhesion molecule 1	19p13.3	8174	-0.0837	-0.0151
129	NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	4q24	4790	-0.0842	-0.0138
130	CCND3	cyclin D3	6p21	896	-0.086	-0.0144
131	GCLC	glutamate-cysteine ligase, catalytic subunit	6p12	2729	-0.0932	-0.0226
132	BLR1	CXCR5 (Chemotactic cytokine) 5	11q23.3	643	-0.102	-0.0357
133	CTSB	cathepsin B	8p22	1508	-0.107	-0.0403
134	CD3G	CD3g molecule, gamma (CD3-TCR complex)	11q23	917	-0.114	-0.0476
135	MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	8q24.21	4609	-0.117	-0.0509
136	CCR5	chemokine (C-C motif) receptor 5	3p21.31	1234	-0.122	-0.0555
137	RELB	v-rel reticuloendotheliosis viral oncogene homolog B	19q13.32	5971	-0.124	-0.0565
138	GCLM	glutamate-cysteine ligase, modifier subunit	1p22.1	2730	-0.132	-0.0646
139	STAT5A	signal transducer and activator of transcription 5A	17q11.2	6776	-0.141	-0.0746
140	CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1)	10q11.1	6387	-0.142	-0.0718
141		tumor necrosis factor receptor superfamily, member 10b	8p22-p21	8795	-0.145	-0.0732
						-0.0784
142	PTGDS	prostaglandin D2 synthase 21kDa (brain)	9q34.2-q34.3	5730	-0.15	-0.0784
142			9q34.2-q34.3 19q13.41	5730 354	-0.15 -0.167	-0.0784
	PTGDS KLK3	prostaglandin D2 synthase 21kDa (brain)	19q13.41		-0.167	
143 144	PTGDS KLK3 TPMT	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase	19q13.41 6p22.3	354 7172	-0.167 -0.172	-0.0961 -0.0992
143	PTGDS KLK3	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1	19q13.41 6p22.3 1p32-p31	354	-0.167 -0.172 -0.175	-0.0961
143 144 145 146	PTGDS KLK3 TPMT VCAM1 TNF	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2)	19q13.41 6p22.3 1p32-p31 6p21.3	354 7172 7412 7124	-0.167 -0.172 -0.175 -0.182	-0.0961 -0.0992 -0.0986 -0.105
143 144 145 146 147	PTGDS KLK3 TPMT VCAM1 TNF CCL14	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14	19q13.41 6p22.3 1p32-p31 6p21.3 17q12	354 7172 7412 7124 6358	-0.167 -0.172 -0.175 -0.182 -0.186	-0.0961 -0.0992 -0.0986 -0.105 -0.103
143 144 145 146 147 148	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invarian	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32	354 7172 7412 7124 6358 972	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188	-0.0961 -0.0992 -0.0986 -0.105 -0.103
143 144 145 146 147 148 149	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta)	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33	354 7172 7412 7124 6358 972 8728	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977
143 144 145 146 147 148 149	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21	354 7172 7412 7124 6358 972 8728 3627	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977 -0.106
143 144 145 146 147 148 149 150	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier)	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13	354 7172 7412 7124 6358 972 8728 3627 7351	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977 -0.106 -0.103
143 144 145 146 147 148 149 150 151	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group)	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13	354 7172 7412 7124 6358 972 8728 3627 7351 960	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101
143 144 145 146 147 148 149 150 151 152 153	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44 BCL2A1	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group) BCL2-related protein A1	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13 15q24.3	354 7172 7412 7124 6358 972 8728 3627 7351 960 597	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101 -0.108
143 144 145 146 147 148 149 150 151 152 153 154	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44 BCL2A1 CD48	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group) BCL2-related protein A1 CD48 molecule	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13 15q24.3 1q21.3-q22	354 7172 7412 7124 6358 972 8728 3627 7351 960 597	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209 -0.22 -0.239	-0.0961 -0.0992 -0.0986 -0.105 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101 -0.108 -0.124
143 144 145 146 147 148 149 150 151 152 153 154 155	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44 BCL2A1 CD48 NR3C1	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group) BCL2-related protein A1 CD48 molecule nuclear receptor subfamily 3, group C, member 1 (glucocorticoid re	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13 15q24.3 1q21.3-q22 5q31.3	354 7172 7412 7124 6358 972 8728 3627 7351 960 597 962 2908	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209 -0.22 -0.239 -0.243	-0.0961 -0.0992 -0.0986 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101 -0.108 -0.124 -0.121
143 144 145 146 147 148 149 150 151 152 153 154 155 156	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44 BCL2A1 CD48 NR3C1 BCL10	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group) BCL2-related protein A1 CD48 molecule nuclear receptor subfamily 3, group C, member 1 (glucocorticoid re B-cell CLL/lymphoma 10	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13 15q24.3 1q21.3-q22 5q31.3 1p22	354 7172 7412 7124 6358 972 8728 3627 7351 960 597 962 2908 8915	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209 -0.22 -0.239 -0.243 -0.292	-0.0961 -0.0992 -0.0986 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101 -0.108 -0.124 -0.121 -0.153
143 144 145 146 147 148 149 150 151 152 153 154 155	PTGDS KLK3 TPMT VCAM1 TNF CCL14 CD74 ADAM19 CXCL10 UCP2 CD44 BCL2A1 CD48 NR3C1	prostaglandin D2 synthase 21kDa (brain) kallikrein-related peptidase 3 thiopurine S-methyltransferase vascular cell adhesion molecule 1 tumor necrosis factor (TNF superfamily, member 2) chemokine (C-C motif) ligand 14 CD74 molecule, major histocompatibility complex, class II invariar ADAM metallopeptidase domain 19 (meltrin beta) chemokine (C-X-C motif) ligand 10 uncoupling protein 2 (mitochondrial, proton carrier) CD44 molecule (Indian blood group) BCL2-related protein A1 CD48 molecule nuclear receptor subfamily 3, group C, member 1 (glucocorticoid re	19q13.41 6p22.3 1p32-p31 6p21.3 17q12 5q32 5q32-q33 4q21 11q13 11p13 15q24.3 1q21.3-q22 5q31.3	354 7172 7412 7124 6358 972 8728 3627 7351 960 597 962 2908	-0.167 -0.172 -0.175 -0.182 -0.186 -0.188 -0.19 -0.203 -0.205 -0.209 -0.22 -0.239 -0.243	-0.0961 -0.0992 -0.0986 -0.103 -0.101 -0.0977 -0.106 -0.103 -0.101 -0.108 -0.124 -0.121

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160	CCL21	chemokine (C-C motif) ligand 21	9p13	6366	-0.335	-0.15
161	CCL19	chemokine (C-C motif) ligand 19	9p13	6363	-0.336	-0.143
162	IFI44L	interferon-induced protein 44-like	1p31.1	10964	-0.354	-0.144
163	CXCR4	chemokine (C-X-C motif) receptor 4	2q21	7852	-0.362	-0.14
164	PRDM2	PR domain containing 2, with ZNF domain	1p36.21	7799	-0.414	-0.147
165	REL	v-rel reticuloendotheliosis viral oncogene homolog (avian)	2p13-p12	5966	-0.422	-0.139
166	IRF2	interferon regulatory factor 2	4q34.1-q35.1	3660	-0.425	-0.13
167	MX1	myxovirus (influenza virus) resistance 1, interferon-inducible prote	i 21q22.3	4599	-0.428	-0.121
168	LTB	lymphotoxin beta (TNF superfamily, member 3)	6p21.3	4050	-0.438	-0.114
169	IRF7	interferon regulatory factor 7	11p15.5	3665	-0.452	-0.106
170	TLR6	toll-like receptor 6	4p14	10333	-0.453	-0.0952
171	BCL2	B-cell CLL/lymphoma 2	18q21.3	596	-0.462	-0.0858
172	BCL2L10	BCL2-like 10 (apoptosis facilitator)	15q21	10017	-0.463	-0.0751
173	CCR7	chemokine (C-C motif) receptor 7	17q12-q21.2	1236	-0.483	-0.0667
174	IRF4	interferon regulatory factor 4	6p25-p23	3662	-0.491	-0.0557
175	CCR2B	chemokine (C-C motif) receptor 2 isoform B	3p21.31	729230	-0.526	-0.0479
176	TFEC	transcription factor EC	7q31.2	22797	-0.67	-0.0404
177	CD69	CD69 molecule	12p13-p12	969	-0.717	-0.0252
178	CCR2A	chemokine (C-C motif) receptor 2 isoform A	3p21.31	729230	-1.13	-0.000728

SUPPLEMENTARY TABLE LEGENDS

Table S1. NF-κB target genes. Genes were collated from an online data base (http://www.NF-kB.org) published works (http://people.bu.edu/gilmore/nf-kb/target/index.html), and careful bioinformatic search. Noncanonical NF-κB target genes (highlighted in yellow) were identified according to previous investigations (11, 14-21).

Table S2. Leading edge core set of NF-κB target genes that are differentially enriched in MALT lymphomas with t(11;18) vs. no translocation. Noncanonical NF-κB target genes (11, 14-21) are highlighted in yellow.

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